

10/16/96

MEMORANDUM

SUBJECT: Terbufos. American Cyanamid's Acute Dietary Risk Analysis Using the Tier III "Monte Carlo" Exposure Model. ID No. 105001. DP Barcode No. D225037.

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In response to HEDs acute dietary risk assessment for terbufos (HED RED chapter dated 10/17/95), American Cyanamid has submitted an acute dietary risk assessment conducted by TAS using the Tier III "Monte Carlo" exposure model.

Background

The Agency's assessment was based on tolerance level residues and the 1977-78 Nationwide Food Consumption Survey; in contrast, the TAS assessment used the USDA Continuing Surveys of Food Intake by Individuals (CSFII) of 1989 through 1992, as well as field trial data in which crops were treated at the maximum rate. The TAS assessment used mean residues from field trials, rather than the tolerance level residues used by the Agency, for blended commodities. Percent crop treated data were used in the TAS assessment. The Monte Carlo analysis was conducted for single serving commodities, instead of using tolerance level residues for all commodities. Rather than using absolute high-end exposure estimates, TAS calculated 95th percentile estimates, and compared these estimates to the established NOEL of 0.005 mg/kg/day for plasma cholinesterase inhibition (dog studies), as well as to the proposed NOEL of 0.04 mg/kg/day based on RBC/brain cholinesterase inhibition (2-generation rat reproduction study).

Discussion

In general, the approach used by American Cyanamid/TAS is sound. However, the analysis departs from the guidelines in two significant ways and, therefore, should be modified.

- 1) TAS used the assumption of mixing/blending of commodities in commerce to justify the use of average point estimates of residues (from field trials) as the residue values for portions of the analysis. The uses of this assumption appear valid. However, they then applied a correction for percent of crop treated to these average values. Where average point estimates are used in acute analyses, they may not be corrected for per cent of crop treated. Therefore, this analysis underestimates the risk by lowering the residues used for mixed/blended forms of the commodities included beyond the intent of the guideline.

- 2) The body of the report gives only the MOEs for the 95th percentile exposure and indicates that this is the appropriate level for use in risk assessment based upon the use of cholinesterase inhibition as an endpoint. Three major difficulties arise with this argument.
 - 1) The use of the 95th percentile is often assumed to be reasonable for unrefined acute analyses because of the many built in conservatisms in the exposure estimates and the hazard assessment. This analysis is highly refined, uses the entire range of field trial residue data for much of the assessment (and includes percent crop treated data in the Monte Carlo portion of the analysis) and includes no tolerances or high end field trial residues to estimate exposure. Therefore, a more conservative approach appears warranted in performing the risk assessment. The assessment underestimates the exposure, which will almost certainly increase when the inappropriate corrections for per cent crop treatment (described in #1 above) are corrected.
 - 2) The suggestion that the 95th percentile is appropriate because the toxicity endpoint is cholinesterase inhibition is not acceptable. At the critical dose level, both plasma AND red blood cell cholinesterase inhibition occurred. Further, Agency policy does not permit the discounting of cholinesterase inhibition as a toxic sign.
 - 3) In reviewing the more detailed tables provided in Appendix 3, the use of the 95th percentile exposure level was necessary to obtain an MOE of 100 for non-nursing infants and all infants (consumers only), even with the use of the many refinements incorporated in this analysis. These two groups achieved acceptable MOEs (>100) at the 97.5th percentile of exposure when using all possible subjects.

RECOMMENDATION

This analysis should be repeated with the omission of the application of percent crop treated to the processed commodities residues and the results reevaluated by the Agency. Use of the 99th percentile exposure level should be considered by the registrant, due to the highly refined nature of the exposure estimates.